

WHAT IS CLAIMED IS:

- 546 B¹
- 5 1. A method for treating a subject with a hyperproliferative disease comprising the steps of:
- 10 (i) identifying a subject with a hyperproliferative disease characterized by alteration or increased expression of a self gene product in at least some of the hyperproliferative cells in said patient; and
- 15 (ii) intradermally administering to said subject an expression construct comprising a self gene under the control of a promoter operable in eukaryotic dendritic cells,
- whereby said self gene product is expressed by dendritic cells and presented to immune effector cells, thereby stimulating an anti-self gene product response.
2. The method of claim 1, wherein said self-gene product is an oncogene.
- 20 3. The method of claim 2, wherein said oncogene is selected from the group consisting of tumor suppressors, tumor associated genes, growth factors, growth-factor receptors, signal transducers, hormones, cell cycle regulators, nuclear factors, transcription factors and apoptic factors.
- 25 4. The method of claim 3, wherein said tumor suppressor is selected from the group consisting of Rb, p53, p16, p19, p21, p73, DCC, APC, NF-1, NF-2, PTEN, FHIT, C-CAM, E-cadherin, MEN-I, MEN-II, ZAC1, VHL, FCC, MCC, PMS1, PMS2, MLH-1, MSH-2, DPC4, BRCA1, BRCA2 and WT-1.

5. The method of claim 3, wherein said growth-factor receptor is selected from the group consisting of FMS, ERBB/HER, ERBB-2/NEU/HER-2, ERBA, TGF- β receptor, PDGF receptor, MET, KIT and TRK.
- 5 6. The method of claim 3, wherein said signal transducer is selected from the group consisting of SRC, ABL, RAS, AKT/PKB, RSK-1, RSK-2, RSK-3, RSK-B, PRAD, LCK and ATM.
- 10 7. The method of claim 3, wherein said transcription factor or nuclear factor is selected from the group consisting of JUN, FOS, MYC, BRCA1, BRCA2, ERBA, ETS, EVII, MYB, HMGI-C, HMGI/LIM, SKI, VHL, WT1, CEBP- α , NFKB, IKB, GL1 and REL.
- 15 8. The method of claim 3, wherein said growth factor is selected from the group consisting of SIS, HST, INT-1/WT1 and INT-2.
9. The method of claim 3, wherein said apoptic factor is selected from the group consisting of Bax, Bak, Bim, Bik, Bid, Bad, Bcl-2, Harakiri and ICE proteases.
- 20 10. The method of claim 3, wherein said tumor associated gene is selected from the group consisting of CEA, mucin, MAGE and GAGE.
11. The method of claim 4, wherein said tumor suppressor product is p53.
- 25 12. The method of claim 1, wherein said expression construct is a viral vector.
13. The method of claim 12, wherein said viral vector is an adenoviral vector, a retroviral vector, a vaccinia viral vector, an adeno-associated viral vector, a polyoma viral vector, an alphavirus vector, or a herpesviral vector.

14. ~~The method of claim 13, wherein said viral vector is an adenoviral vector.~~

5 4 6 B² 15. ~~The method of claim 14, wherein said adenoviral vector is replication defective.~~

5

16. The method of claim 15, wherein the replication defect is a deletion in the E1 region of the virus.

17. The method of claim 16, wherein the deletion maps to the E1B region of the virus.

10

18. The method of claim 17, wherein the deletion encompasses the entire E1B region of the virus.

19. The method of claim 18, wherein the deletion encompasses the entire E1 region of the virus.

15

20. The method of claim 1, wherein said promoter is selected from the group consisting of CMV IE, human or murine dectin-1, human or murine dectin-2, human CD11c, mammalian F4/80 and human or murine MHC class II.

20

21. The method of claim 20, wherein said promoter is CMV IE.

22. The method of claim 1, wherein said expression vector further comprises a polyadenylation signal.

25

23. ~~The method of claim 1, wherein said hyperproliferative disease is cancer.~~

24. The method of claim 23, wherein said cancer is selected from the group consisting of lung, head, neck, breast, pancreatic, prostate, renal, bone, testicular, cervical, gastrointestinal, lymphoma, brain, colon, skin and bladder.

30

25. The method of claim 1, wherein said hyperproliferative disease is selected from the group consisting of RA, IBD, OA, leiomyomas, adenomas, lipomas, hemangiomas, fibromas, melanomas, restenosis, pre-neoplastic lesions in the lung and psoriasis.

5

26. The method of claim 1, wherein said expression construct is administered via injection.

27. The method of claim 26, further comprising multiple injections.

10

28. The method of claim 26, wherein the injection is performed local to a hyperproliferative or tumor site.

15

29. The method of claim 26, wherein the injection is performed regional to a hyperproliferative or tumor site.

30. The method of claim 26, wherein the injection is performed distal to a hyperproliferative or tumor site.

20

31. The method of claim 1, wherein intradermal administration is via continuous infusion.

32. The method of claim 1, wherein said subject is a human.

25

33. The method of claim 1, wherein said immune effector cells are CTLs.

34. The method of claim 1, further comprising administering to said subject at least a first cytokine.

35. The method of claim 34, further comprising administering to said subject a second cytokine, different from said first cytokine.

5 36. The method of claim 34, wherein said cytokine is selected from the group consisting of GM-CSF, IL-4, C-KIT, Steel factor, TGF- β , TNF- α and FLT3 ligand.

37. The method of claim 34, wherein said cytokine is administered as a gene encoded by said expression construct.

10 38. A method for treating a pathogen-induced disease in a subject comprising the steps of:

- 15
- (i) identifying a subject with a pathogen-induced disease characterized by alteration or increased expression of a pathogen gene product in at least some of the pathogen-induced cells in said patient;
 - (ii) intradermally administering to said subject an expression construct comprising a pathogen gene under the control of a promoter operable in eukaryotic dendritic cells;
 - (ii) infecting said dendritic cells with an adenoviral vector comprising a pathogen gene product under the control a promoter operable in eukaryotic cells; and
 - 20 (iii) administering the adenovirus-infected dendritic cells to said subject,

25 whereby said pathogen gene product is expressed by dendritic cells and presented to immune effector cells, thereby stimulating an anti-pathogen gene product response.

39. The method of claim 38, wherein said dendritic cells are obtained from peripheral blood progenitor cells.

40. The method of claim 38, further comprising multiple administrations of adenovirus-infected dendritic cells.

41. The method of claim 38, wherein said pathogen is selected from the group consisting of bacterium, virus, fungus, parasitic worm, amoebae and mycoplasma.

42. The method of claim 41, wherein said bacterium is selected from the group consisting of richettsia, listeria and histolytica.

43. The method of claim 41, wherein said virus is selected from the group consisting of HIV, HBV, HCV, HSV, HPV, EBV and CMV.

44. The method of claim 41, wherein said fungus is selected from the group consisting of hitoplasma, coccidis, immitis, aspargillus, actinomyces, blastomyces, candidia and streptomyces.

45. The method of claim 38, wherein said expression construct is a viral vector.

46. The method of claim 45, wherein said viral vector is an adenoviral vector, a retroviral vector, a vaccinia viral vector, an adeno-associated viral vector, a polyoma viral vector, an alphavirus vector, or a herpesviral vector.

47. The method of claim 46, wherein said viral vector is an adenoviral vector.

48. The method of claim 47, wherein said adenoviral vector is replication-defective.

49. The method of claim 48, wherein the replication defect is a deletion in the E1 region of the virus.

50. The method of claim 49, wherein the deletion maps to the E1B region of the virus.

51. The method of claim 50, wherein the deletion encompasses the entire E1B region of the virus.

5 52. The method of claim 51, wherein the deletion encompasses the entire E1 region of the virus.

53. The method of claim 38, wherein said promoter is selected from the group consisting of CMV IE, human or murine dectin-1, human or murine dectin-2, human
10 CD11c, mammalian F4/80 and human or murine MHC class II.

54. The method of claim 53, wherein said promoter is CMV IE.

55. The method of claim 38, wherein said expression vector further comprises a
15 polyadenylation signal.

56. The method of claim 38, wherein intradermal administration is by injection of the expression construct.

20 57. The method of claim 56, further comprising multiple injections.

58. The method of claim 56, wherein the injection is performed local to a pathogen-induced disease site.

25 59. The method of claim 56, wherein the injection is performed regional to a pathogen-induced disease site.

60. The method of claim 56, wherein the injection is performed distal to a pathogen-induced disease site.

30

add a²7